

REMARKS

Claims 1, 3-4, 7, and 10-13 were pending in this application. No claims have been amended, canceled or added. Hence, claims 1, 3-4, 7, and 10-13 remain pending. Reconsideration and allowance of the present application based on the following remarks is respectfully requested.

35 U.S.C. §103 Rejections

1. Rejection Over Kopf-Sill in view of Crabtree

Claims 1, 3, and 4 stand rejected under 35 U.S.C. §103 (a) as being unpatentable over U.S. Pat. No. 6,613,512 or U.S. Pat. No. 6,524,790 (collectively “Kopf-Sill” in light of their duplicate disclosure) in view of Crabtree et al., Anal. Chem. 1999, 2130-2138 (hereinafter “Crabtree”). Applicants respectfully traverse the rejection for at least the reasons which follow.

Applicants’ claimed invention is a method for determining a characteristic parameter of an analyte independent of a flow velocity of the analyte, wherein measurement of the characteristic parameter of the analyte is capable of being influenced by or dependent on the velocity of the analyte, said method comprising:

- (a) transporting a fluid medium comprising the analyte from a first position to a second position of a fluid flow channel of a fluidic device;
- (b) measuring the characteristic parameter of the analyte within the fluid flow channel at a plurality of different detection zones separated along a flow path of the analyte in between the first and the second positions; and
- (c) determining a velocity dependence of the measurement of the characteristic parameter and determining the characteristic parameter of the analyte independent of the flow velocity of the analyte by using the measured characteristic parameters of step (b) and normalizing the measurement by substantially eliminating the velocity dependence of the measurement.

Applicants’ claimed method is an important innovation the way that one or more analytes are measured in fluidic systems and, as such, it opens the door for the implementation of

a much greater variety of fluidic and microfluidic analytical methodologies. The claimed method greatly reduces the variability in signal measurements of an analyte when the measured signal is affected by fluctuations in the flow rate. As discussed below, Applicants' claimed invention is novel and nonobvious over Kopf-Sill either alone or in combination with any of the cited references.

The Office Action alleges that Kopf-Sill et al. disclose methods and microfluidic devices to measure reactants and reaction products while considering velocity, that reactants and products with different velocities are measured in a microfluidic channel, that in one embodiment the fluid samples are transported from a first position to a second position by electroosmotic flow, and that time dependent data generated is processed to include baseline subtraction and masking for accurate measurements of the analyte of interest. It is further alleged that multiple detection positions/zones are taught at two different time points in figure 1 of Kopf-Sill, that time difference and velocity are utilized in an equation to accurately measure the characteristic of interest in the analyte, that the various reactants and products can be assessed serially (individually) or simultaneously in the methods, and that Kopf-Sill teaches the step of normalizing or eliminating the velocity component in reaction measurements.

The Office Action relies on the Crabtree reference for allegedly disclosing a particle detection method which converts multiple-point (Shah function) time dependent measurements into fluorescence frequencies allowing for the viewing of analyte speed. It is further alleged that the SCOFI principle is utilized in a system comprising multiple detection slits that detect the sample fluorescence at varied times during the flow of sample through a column or channel, that (in figure 1) the particle is constantly interrogated at a number of evenly spaced points (slits or zones) along the column or channel simultaneously by a single detector and that the signals measured from all of these points along the column are summed. It is further alleged that the process advantageously isolated the analyte peak from interferences such as baseline drift and line noise. The Office Action concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use dual detection zones, slits, spaces zones (plurality of detection zones) as taught by Crabtree in either method of Kopf-

Sill because Crabtree taught that dual detection zones, slits, spaced zones advantageously isolated the analyte peak from interferences such as baseline drift and line noise and that one of ordinary skill in the art would have been motivated to utilize dual detection zones in order to more accurately detect the particles of interest.

Applicants wish to emphasize to the Office that Applicants' claimed invention is a specialized method of analysis utilizing data analysis of a plurality of detection zones to arrive at an understanding of the flow-analyte characteristic parameter relationship. Kopf-Sill teaches an analysis of a signal at a single detection zone¹ and the use of that data solely for the determination of the rate or extent of a reaction or assay through the measurement of reactants or products. The Kopf-Sill data obtained from the single detection site cannot be analyzed as required in Applicants' claimed invention and there is no teaching in Kopf-Sill as to how one would analyze data from a plurality of detection zones to substantially eliminate the velocity dependence of the measurement. Crabtree teaches a form of Fourier transform analysis for generating electropherograms. The Crabtree methodology relates exclusively to a technique for resolving multiple peaks in an electrophoresis system. Although the Office Action quotes the advantages recited in the Crabtree abstract, it does not note the following sentence in the Crabtree abstract that "[r]esolution is somewhat inferior to that seen in single point detection..." Crabtree's methodology does not relate in any way to the analysis of analyte data to substantially eliminate the velocity dependence of the measurement. Furthermore, Crabtree's acknowledgement of its own deficiencies vis-à-vis resolution would discourage one skilled from attempting its application to a wholly different analytical problem. Thus, there is nothing in Kopf-Sill that would lead one of ordinary skill in the art to develop a multiple detection zone technique and there is nothing in Crabtree's Fourier transform detection methodology that would lead one of ordinary skill in the art to develop a method to substantially eliminate the velocity dependence of an analyte measurement.

¹ It is presumed that the statement in the first sentence of the second paragraph on page 4 of the Office Action is recognized by the Office as being in error. Figure 1 of Kopf-Sill does not teach multiple detection positions/zones.

For at least these reasons, it is submitted that the claims are patentable over Kopf-Sill in view of Crabtree, and withdrawal of this rejection is respectfully requested.

2. Rejection Over Kopf-Sill and Crabtree in view of Squire

Claim 7 stands rejected under 35 U.S.C. §103(a) as unpatentable over Kopf-Sill in view of Crabtree, and further in view of *J. Microscopy*, 197(2) 2/2000, 136 – 149 (hereinafter “Squire”). This rejection is respectfully traversed. Whatever else Squire may disclose, it does not remedy the deficiencies of Kopf-Sill and Crabtree, as described above. As such, it is submitted that the claims are patentable over the cited art, and withdrawal of this rejection is respectfully requested.

3. Rejection Over Kopf-Sill and Crabtree in view of Armstrong

Claims 10-13 stand rejected under 35 U.S.C. §103(a) as unpatentable over Kopf in view of Crabtree, and further in view of *Cytometry*, 40:102-108, 2/2000 (hereinafter “Armstrong”). This rejection is respectfully traversed. Whatever else Armstrong may disclose, it does not remedy the deficiencies of Kopf-Sill and Crabtree, as described above. As such, it is submitted that the claims are patentable over the cited art, and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

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PATENT

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,

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